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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,858	08/14/2008	Leonardo Marchitto	291460US0PCT	5966

22850 7590 07/29/2011

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EXAMINER	
KRASS, FREDERICK F	
ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
07/29/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)
	10/582,858	MARCHITTO ET AL.
	Examiner	Art Unit
	RYAN C. SMITH	1612

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *7,8 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/14/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Claims

Claims 1-10 are currently amended.

Claims 7-8 and 10 are withdrawn from further consideration.

Claims 1-6 and 9 are considered on their merits in this Official Action.

Election/Restrictions

Applicant's reply dated 05/04/2011 to the restriction, whereby applicant's election with traverse of the species glycine and water-soluble granulate form is acknowledged. Claims 1-6 and 9 will be examined in this Official Action. Claims 7-8 and 10 are withdrawn from further consideration as being drawn to nonelected species. Election was made **with** traverse in the reply filed on 05/04/2011

Applicant's arguments

Applicant argued that the Examiner has not provided a single reason or example why the species are patentably distinct.

Examiner's Response

The species are independent or distinct because each species is structurally distinct from another. In addition, these species are not obvious variants of each other based on the current record. Since each species is structurally distinct form one another, a separate search would have to be conducted on each species. The search will be based on the structure and not the function of the species.

If, the applicant states **on the record** that the species are obvious variants of one another the Examiner will withdrawal the election of species requirement. In essence if the applicant states that the species are obvious variants the Examiner, in finding a

single disclosed species, the species will anticipate or render obvious all of the claimed species.

The requirement is still deemed proper and is therefore made **FINAL**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-6 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Santus et al (US 5,296,236).

The claims are drawn to an oral composition.

Santus et al (hereinafter Santus) teaches a controlled release pharmaceutical dosage form, including: (a) microgranules of a pharmaceutical and an excipient; (b) a plurality of polymeric lipidic and wax-like coatings applied to the microgranules, the coated microgranules having dimensions which allow suspension of the coated microgranules in a liquid administration vehicle; and (c) a liquid administration vehicle for the coated microgranules, the vehicle including an effective amount of the pharmaceutical in a form immediately available upon ingestion (abstract).

In addition to the amount of coated microgranules containing the dose of controlled release active ingredient, the elements constituting the vehicle for form (a) are: (1) - a dose of active principle in solution, forming a readily absorbable fraction; (2)

suspending and structural agents such as cellulose esters, microcrystalline cellulose, alginic acid derivatives, polyvinyl pyrrolidone derivatives; (3) sugars, such as sucrose and sorbitol; (4) buffers such as citric acid and sodium citrate, glycine and hydrochloric acid, sodium and potassium phosphates; (5) preservatives and bacteriostatic agents such as p-hydroxybenzoic acid esters; (6) aromatizing and sweetening agents such as saccharine and others; and (7) water or mixtures of water and solvents such as glycols, alcohols, glycerin (col. 6, lines 13-27). Note that instant claim 1 described the use of glycine in an oral formulation.

Santus also claims the controlled release pharmaceutical dosage form wherein said pharmaceutical is selected from the group consisting of theophylline, ketorolac tromethamine and naproxen (claim 2). Note that the claim language teaches individual and combination therapies of tromethamine and naproxen can be used in combination in an oral pharmaceutical dosage form.

Santus also teaches the kneading liquid may be water or a solvent miscible with water, as for example ethyl alcohol and other commonly used alcohols, or a water-alcohol mixture. According to the invention, the granulate is then coated, in successive phases and according to known coating techniques, with films of different compositions. Note that the granules taught in Santus are water soluble. Instant claim 9 describes the use of water soluble granules.

It would have been obvious to one of ordinary skill in the art to combine tromethamine and an NSAID because Santus teaches a composition that can comprises tromethamine and an NSAID (naproxen).

Moreover, the MPEP states "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In the instant case the use of tromethamine and an NSAID is taught in Santus (claim 2). Thus the combination of these drugs could be achieved through no more than routine experimentation to provide a drug formulation that comprises the medicinal qualities of tromethamine and naproxen.

This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman*, 1943 C.D. 518. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In the instant case, any NSAID could be included with tromethamine in order to have a therapeutic effect. Unless applicant shows evidence to the contrary one of ordinary skill in the art could use any NASAID in combination with tromethamine to arrive at an additive therapeutic effect.

The MPEP states "Generally differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. Where the general condition of a claim are disclosed in the prior art, it is not inventive to discover the optimal or workable ranges by routine experimentation." See MPEP 2144.05. Instant

claims 2-6 describe the various concentrations by weight of the glycine and tromethamine in an oral composition. However, one of ordinary skill in the art could readily alter the concentration depending on specific formulation desired. Thus, unless applicant shows teaching to the contrary, instant claims 2-6 do not rise beyond that of a general condition achieved through obvious experimental optimization.

Claims 1-6 and 9 are rendered obvious.

1. Claims 1-6 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penkler et al (WO 97/18245) in further view of Ream et al (US 2003/0003152 A1).

The claims are drawn to a composition.

Penkler et al (hereinafter Penkler) teaches an inclusion complex of naproxen or a pharmaceutically acceptable salt thereof, a beta-cyclodextrin and a hydroxylamine, and to pharmaceutical compositions containing the inclusion complex (page 1). Moreover, Penkler specifically teaches tromethamine and an NSAID in a water soluble granular form (Examples 1 and 3). Moreover, Penkler teaches a ratio of 1:10:1 of naproxen to tromethamine to cyclodextrin (Example 3). Penkler also teaches a ratio of 1:1:1 of naproxen to tromethamine to cyclodextrin (Example 1).

Penkler does not specifically teach the use of glycine.

Ream et al (hereinafter Ream) teaches a composition that includes a coating having a medicament or agent. The medicament or agent is present within the coating that surrounds a tableted center. The tableted center is defined by compressible excipients (abstract). Ream also teaches an embodiment, the coating includes a

masking agent to assist in improving the organoleptic properties of the coating containing the medicament. The masking agent may be chosen from the group consisting of: sucralose; zinc gluconate; ethyl maltol; glycine; acesulfame-K; aspartame; saccharin; fructose; xylitol; spray dried licorice root; glycerrhizine; dextrose; sodium gluconate; glucono delta-lactone; ethyl vanillin; vanillin; normal and high-potency sweeteners; and a variety of appropriate flavors (para [0022]). Moreover, in the case of a moderately bitter active ingredient, such as caffeine, one would use ingredients such as glycine, ethyl maltol, zinc gluconate, licorice root powder, high-intensity sweeteners, etc. (para [0063]).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Penkler and Ream to arrive at a composition with tromethamine, an NSAID and glycine because glycine can be used to mask bitter taste in oral pharmaceutical preparations comprising bitter tasting drugs (para [0063]).

There is a reasonable expectation of success because the increased association constant of the ternary complex retards dissociation of naproxen in the oral cavity and thereby masks its taste. Thus, the first important advantage of the complex of the invention is taste-masking (page 15, lines 1-5).

The MPEP states “Generally differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. Where the general condition of a claim are disclosed in the prior art, it is not inventive to discover the optimal or workable ranges by routine experimentation.” See MPEP 2144.05. Instant

claims 2-6 describe the various concentrations by weight of the glycine and tromethamine in an oral composition. However, one of ordinary skill in the art could readily alter the concentration depending on specific formulation desired. Thus, unless applicant shows teaching to the contrary, instant claims 2-6 do not rise beyond that of a general condition achieved through obvious experimental optimization.

Claims 1-6 and 9 are rendered obvious.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RYAN C. SMITH whose telephone number is (571)270-5250. The examiner can normally be reached on Mon. - Thurs. 8 am - 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/R. C. S./
Examiner, Art Unit 1612

/Anish Gupta/
Primary Examiner, Art Unit 1654